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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/891,943	06/26/2001	W. Michael Gallatin	27866/37524	2656

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MARSHALL, GERSTEIN & BORUN LLP
6300 SEARS TOWER
233 S. WACKER DRIVE
CHICAGO, IL 60606

EXAMINER

GAMBEL, PHILLIP

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 06/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/891,943	GALLATIN ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11,12 and 14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11,12,14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission filed on 5/6/04 has been entered.

Applicant's amendment, filed 5/6/04, has been entered.

Claims 11 and 12 have been amended.

Claims 11, 12 and 14 are pending.

Claims 1-10 and 13 have been canceled.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.

This Action will be in response to applicant's amendment, filed 5/6/04.

The rejections of record can be found in the previous Office Actions.

3. The filing date of the instant claims is deemed to be the filing date of parent application USSN 08/943,363, filed 10/3/97. It is noted that previous priority applications USSNs 08/605,672; 08/362,652; 08/2886,889; and 08/173,497 do not appear to provide for methods of modulating TNF α release from splenic phagocytes with alphaD-specific antibodies as well as the 205C/205E alphaD-specific antibodies. If applicant desires priority prior to 1/1/91; applicant is invited to point out and provide documentary support for the priority of the instant claims. Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

It has been noted that applicant's amendment, filed 8/14/03, has updated the status of the priority documents, but still maintains a claim for priority back to USSN 08/173,497, filed 12/23/93.

4. As pointed as previously, applicant's amendment, filed 8/14/03, indicates that formal drawings have been submitted, however no such drawings appear for the scanned application.

Given the changes to Image File Wrapper at the USPTO, the examiner does not request another submission of drawings at this time. Such requirements that would be in compliance with 37 CFR 1.84 as set forth in the form PTO-948, mailed 2/11/03, will be considered and addressed if this application is placed in condition for allowance.

The examiner apologizes for any inconvenience to applicant in this matter.

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5. Claims 11, 12 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "alphaD specificity encoded by the amino acid sequence SEQ ID NO: 2 or the nucleic acid sequence SEQ ID NO: 1" disclosed in the specification and now claimed (and priority applications) as-filed, does not reasonably provide enablement for any "alphaD specificity", including "a polynucleotide that hybridizes to the complement of the polynucleotide of (a) or (b), under conditions that include a final wash in 1X SSC/0.1% SDS at 65° C. and wherein said alphaD polypeptide retains a biological activity of alphaD" to be the specificity targeted in the claimed methods to modulate TNF α release from macrophages or phagocytes in order to inhibit immune responses for the reasons of record.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims. molecule.

Applicant's amendment, filed 5/6/04, have been fully considered but are not found convincing essentially for the reasons of record.

In the absence of a testable functional or biological property (or properties) in the context of the recitation of "a polynucleotide that hybridizes to the complement of the polynucleotide of (a) or (b), under conditions that include a final wash in 1X SSC/0.1% SDS at 65° C." set forth in claim 11(c), there are insufficient characteristics that would enable the claimed "alphaD" specificity. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe nor enable any "alphaD" hybridizing nucleic acid specificity.

While applicant is relying upon the disclosure of certain biological activities and the claimed recitation of a "biological activity" (but the lack of a recitation of any specific "biological activity") of a limited representative number of species to support an entire genus, the recitation of any hybridizing nucleic acid does not provide sufficient predictability and structural constraints to the claimed "alphaD" specificity. The instant invention encompasses targeting any "alphaD" to modulate TNF α release from macrophages or phagocytes in order to inhibit immune responses, yet the instant specification does not provide sufficient guidance and direction how to make and use any hybridizing nucleic acid in the absence of testable functional attributes, as currently encompassed by the claims. For example, the specification does not provide for the correlation between the chemical structure and the function of the genus of "alphaD molecules", currently encompassed by the claimed invention. The reliance on the disclosed limited examples of certain known sequences that encode "alphaD" indicated above and disclosed in the specification as filed does not provide sufficient enablement of any protein encoded by protein encoded by "alphaD molecule encoding hybridizing nucleic acids", as currently claimed. It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biology, expression and activities.

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Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality (e.g. ligand or receptor; integrin) requires a knowledge of and guidance with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which a polypeptide's structure relates to its functional usefulness. However, the problem of predicting polypeptide structure from mere sequence data of a single amino acid sequence and in turn utilizing predicted structural determinations to ascertain binding or functional aspects ligands and receptors and finally what changes can be tolerated with respect thereto is complex and well outside the realm of routine experimentation. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Because of the lack of sufficient guidance and predictability in determining which structures would lead to "alphaD" encoding nucleic acids other than those disclosed in the specification as filed with the desired properties and that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) was not well understood and was not predictable (e.g. see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.); it would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of proteins encoded by "alphaD" encoding hybridizing nucleic acids targeted by the claimed methods to modulate TNF α release from macrophages or phagocytes in order to inhibit immune responses.

Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

In the absence of sufficient guidance and direction to the structural and functional analysis, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue to make and use proteins encoded by "alphaD" hybridizing nucleic acids other than those disclosed in the specification as filed and now claimed as the target specificity in the claimed methods OR adding testable functional properties associated with the recitation of "a polynucleotide that hybridizes to the complement of the polynucleotide of (a) or (b), under conditions that include a final wash in 1X SSC/0.1% SDS at 65° C." set forth in claim 11(c).

Without sufficient guidance, making and using proteins encoded by "alphaD" hybridizing nucleic acids other than the such proteins encoded by "alphaD" hybridizing nucleic acids recited in the context of testable functional attributes disclosed in the specification as filed as the target specificity in the claimed methods would have been unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

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Again applicant is invited to amend the claims to recite testable functional attributes with respect to claim 11(c). Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06. In addition, applicant is invited to indicate the date of priority for such language.

While applicant's arguments rely upon certain binding properties of alphaD disclosed in the specification as filed, the claims have not been amended to recite any specific "biological activities" that may be tested that can define the claimed alphaD specificity.

Applicant's reliance upon disclosed but unclaimed limitations have not been found persuasive.

6. Claim 14 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention

Claim 14 is rejected as being dependent on a canceled claim.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

7. Claim 11, 12 and 14 are rejected under 35 U.S.C. § 102(b) as being anticipated by Gallatin et al. (U.S. Patent No. 5,437,958) (see entire document) for the reasons of record.

Applicant's arguments, filed 5/6/04, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same of record.

Although applicant has acknowledged that Gallatin discloses the use of anti- α D antibodies for treating immune or inflammatory responses, Gallatin does not give any particular examples nor suggest modulating TNF- α release. Applicant continues to rely upon the provision of Feliciani et al. (Int. J. Immunopathol. Pharmacol. 12: 55-61, 1999), Takashi et al. (Ann. Allergy Asthma Immunol. 50: 150-155, 2000) and Huang et al. (J. Exp. Med. 193: 713-725, 2001) to indicate that not all inflammatory conditions are associated with TNF- α release.

In contrast to applicant's assertions, Gallatin et al. teach methods of treating immune or inflammatory responses with antibodies that bind alphaD (see Background of the Invention, including column 3, paragraph 2; Brief Description of the Invention; Detailed Description of the Invention). Gallatin et al. provides further guidance that the nature of the inflammatory conditions associated with macrophages include atherosclerosis, multiple sclerosis and diabetes (column 5, paragraph 5), which are consistent with the instant disclosure (pages 14-15, overlapping paragraph and page 16, paragraph 1).

The claimed functional limitations of modulating TNF α release from macrophages or phagocytes with alphaD-specific antibodies, including the α D I-domain specificity, would be inherent properties of the referenced methods to treat immune or inflammatory responses with inhibitory alphaD-specific antibodies.

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It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

Even though the claims are drawn to a mechanism by which the alphaD-specific antibodies inhibit immune or inflammatory responses, the claimed methods do not appear to distinguish the prior art teaching the same or nearly the same methods to achieve the same end result. The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Applicant has not provided sufficient objective evidence to distinguish the prior art methods that rely upon the same alphaD-specific antibodies to treat the same targeted patient populations from that encompassed by the instant claimed methods.

Applicant's arguments are not found persuasive.

8. Claims 11, 12 and 14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over
claims 1-10 of U.S. Patent No. 6,251,395 and
claims 1-9 of U.S. Patent No. 6,432,404 for the reasons of record.

Applicant's arguments, filed 8/14/03, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's amendment, filed 5/6/04, does not address this rejection of record.

As pointed out previously, although applicant acknowledges that the patent claims recite methods for inhibiting macrophage infiltration or locomotor injury in the CNS using antibodies to alphaD, applicant asserts in conjunction with Flugel et al. (Eur. J. Immunol 31: 11-22, 2001 and Huang et al. (J. Exp. Med 193: 713-726, 2001) that the administration of anti-alphaD antibodies could inhibit macrophage infiltration into the brain by a number of mechanisms.

Given that the patented claims are drawn to achieving the same or nearly the same endpoints of inhibiting macrophage infiltration, including the 217L and 226H antibody specificities, such patented claims would anticipate the instant methods of inhibiting the same or nearly same macrophage populations. The present claimed functional limitations of modulating TNF α release from macrophages or phagocytes with alphaD-specific antibodies would be inherent properties of the patented methods to inhibit locomotor damage following spinal cord injury or inhibiting inflammation at the site of a central nervous system injury with alphaD-specific antibodies.

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Applicant's arguments of record have not been found persuasive.

9 No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
June 28, 2004